REMARKS

Claims 1, 6, 12-20, 23-24, 26-27, and 31-35 are pending and claims 1, 31 and 35 have been amended herein. Support for the amendments to claims 1, 31 and 35 can be found in the specification as filed and in originally filed claims 1 and 31. No new matter has been added by these amendments.

Telephone Interview.

Applicants thank the Examiner for the courtesy of the telephone interview that was held on January 15, 2003 with Applicants' representatives. Applicants understand that the Examiner indicated that the present amendments to the claims will overcome the 35 U.S.C. § 112 second paragraph rejections, as set forth in the Final Office Action. As suggested by the Examiner, Applicants file herewith a Declaration under 37 C.F.R. § 1.132 from Dr. Thomas P. Jarvie, a named inventor in the instant application, in order to address the remaining 35 U.S.C. § 102(b)/103(a) rejections.

Drawings

The Examiner has indicated that the Official Draftsperson has checked boxes 5, 10, and 12. Applicants have submitted Formal Drawings to the Official Draftsperson to correct these deficiencies. A copy of the as-filed formal Drawings is provided here for the Examiner's convenience.

Claim Rejections

35 U.S.C. § 112, second paragraph.

Claims 1 and 35 have been rejected under 35 U.S.C. § 112, second paragraph as being incomplete for missing essential elements, the Examiner stating that "the omitted elements are: showing that the bond between hybrid ligand A and the predetermined target is a irreversible (covalent) bond." (Office Action at page 2). As amended, claim 1(c) recites: "(c) permitting the hybrid ligand to bind irreversibly covalently the first hybrid protein through ligand A and the second hybrid protein through ligand B so as to activate the expression of the reporter gene."

Similarly, as amended, claim 35 (c) recites "permitting the hybrid ligand to bind irreversibly covalently the first hybrid protein through ligand A and the second hybrid protein through ligand B so as to activate the expression of the reporter gene, thereby reducing a three-hybrid system to a two-hybrid system."

Applicants contend that, because "irreversible covalent" is a specific claim limitation, there is no need for the specification to show that the bond is irreversible or to demonstrate how to determine that the bond is irreversible, as required by the Examiner. (*See* Office Action at page 3). Rather, these bonds are irreversible because the claim scope limits them to be irreversibly covalent.

Moreover, those skilled in the art will recognize that, because the energy required to break or rearrange them are much greater than the thermal energy available at room temperature (25°C) or at body temperature (37°C), covalent bonds tend to be very stable (i.e., irreversible). *See* Lodish, et al., Eds., Molecular Cell Biology, 4th ed., Chpt. 2.1 (1999).

In addition, Applicants enclose herewith a Declaration under 37 C.F.R. § 1.132 from Dr. Thomas P. Jarvie, a named inventor in the instant application, which states that covalent bonds are irreversible under physiological conditions (*See, e.g.*, ¶ 6).

Therefore, Applicants contend that claims 1 and 35 as amended, include the step of ligand A of the hybrid ligand binding irreversibly covalently to the first hybrid protein. Thus, this rejection should be withdrawn.

35 U.S.C. § 102(b)/103(a)

Claims 1, 6, 12, 17, 19, 20, 23-24, 31-32 and 35 have been rejected under 35 U.S.C. § 102(b) as anticipated by, or in the alternative, under 103(a) as being obvious over United States Patent No. 5,928,868 ("Liu") in combination with Licitra et al. (PNAS USA 93: 12817-21 (1996) ("Licitra"). According to the Examiner, "Figure 3 of the specification refers to the mechanism of Asprin and its analogs with cyclooxygenase. Neither the figure nor the description of the figures disclose that the bind is irreversible covalent." (Office Action, at page 6). The Examiner further contends "Applicants have not shown how and why the bond between the ligand A and the target of the instant claimed method is different from the prior art" (Office Action, paragraph bridging pages 6-7). Applicants traverse.

Applicants have herewith amended independent claims 1, 31, and 35 so that these claims recite that ligand A forms an irreversible covalent bond with the predetermined target. This limitation is neither taught nor suggested by either Liu or Licitra or the combination thereof. Moreover, the claimed methods for identifying a cellular component to which a small molecule is capable of binding are nonobvious improvements of the methods disclosed by Liu and Licitra. To this end, Applicants submit herewith the declaration of Dr. Thomas P. Jarvie, one of the named inventors of the instant application, which demonstrates the novelty and nonobviousness of the claimed invention. (Jarvie Decl. ¶ 7 and 9).

Specifically, Dr. Jarvie describes the mechanism of action of the chemical hybrid system of the present invention and distinguishes the present invention from the three hybrid system Liu and Licitra. (See Jarvie Decl. ¶ 5-8). According to Dr. Jarvie, by having Ligand **A** form an irreversible covalent bond with its target **X** fusion protein, the affinity of the binding between Ligand **B** and its target **Y** fusion protein can be measured, unlike the three hybrid system taught by Liu and Licitra. (See Jarvie Decl. ¶ 7). As stated by Dr. Jarvie and shown in schematic ii, once Ligand **A** forms an irreversible covalent bond with its target **X** fusion protein, only a single ligand-target interaction between Ligand **B** and its target **Y** fusion protein remains; thus, the affinity of this single ligand-target interaction can be determined, in contrast to the three hybrid system taught by Liu and Licitra, in which there are two ligand-target interactions of variable affinity, precluding determination of the affinity of either interaction. (See Jarvie Decl. ¶ 7). Thus, contrary to the Examiner's contention, Applicants have explained the differences between the three hybrid system of the present invention and that of Liu and Licitra.

Dr. Jarvie also notes that the methods of the instant invention cause a reduction in the system noise caused in the methods of Liu and Licitra, and allows for the use of lower concentrations of the hybrid ligand (See Jarvie Decl. ¶ 9). Moreover, Dr. Jarvie states that the chemical hybrid system of the present invention is more effective, more economical, and has greater functional capacity (*e.g.*, the ability to measure the K_d of the binding of Ligand **B** to the target **Y** fusion protein) than the methods of Liu and Licitra. (See Jarvie Decl. ¶ 9).

Thus, for all of the foregoing reasons, Applicants contend that the instant claims, as amended herein, are neither anticipated by nor obvious over Liu and Licitra, either alone or in

combination.

35 U.S.C. § 112, first paragraph.

Claims 1 and 35 have been rejected under 35 U.S.C. § 112, first paragraph for lack of written description, the Examiner stating that the deleted limitation "covalent" and "covalently" is not supported in the specification. (Office Action at page 4). Applicants note that claims 1, 31 and 35 have been amended herein to recite the limitations "irreversible covalent" and "irreversibly covalently." Thus, Applicants assert that claims 1, 31 and 35, as amended herein, are fully supported by the specification as filed. As acknowledged by the Examiner during the telephone interview, Applicants assert that this amendment overcomes this rejection. Thus, this rejection can be withdrawn.

CONCLUSION

Applicants submit that the Examiner's rejections have been overcome based on the enclosed amendments and remarks. Applicants therefore respectfully request that the pending claims be found allowable at this time. Should any questions or issues arise concerning the application, the Examiner is encouraged to contact Applicants' undersigned attorney at the telephone number indicated below.

Respectfully submitted,

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